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Molecular Therapy

Redemption for the Field of Oncolytic Virotherapy

The field of targeted and transgene-armed oncolytic viruses has been through a cycle of boom (mid-1990s) and bust (the early 2000s). In January 2011, however, Amgen—the biggest independent biotechnology company in the world—jumped headfirst into the field by acquiring Biovex for $425 million and promising potential success-based milestone payments of up to $1 billion moving forward. Biovex's targeted and transgene-armed oncolytic virus Oncovex is already in a randomized phase III trial for melanoma and will soon be entering a phase III trial for head and neck cancer. The prospects for therapeutic success of oncolytic virotherapy were no better the day after this announcement. Nevertheless, validation of the field by a major international biopharmaceutical company has been lacking, and the move by Amgen highlights the redemption of the oncolytic virotherapy field that has occurred over the past few years.

As scientists, we take great pride in our objectivity. We strive to be data driven, emotionally detached, and statistically rigorous. Indeed, the ultimate power of science is its self-correcting capacity. The development of novel therapeutic approaches to human disease often starts with a confusing or unexpected finding. However, new ideas can be so compelling that our deeply ingrained scientific skepticism is temporarily suspended, despite a relative paucity of data. During the subsequent boom phase, industry typically enters the picture and throws millions of dollars at scientists or start-up companies with the aim of exploiting the novel technology. However, once these approaches reach the unpredictable world of clinical testing, new hurdles are often identified. Not every patient is cured. Panic sets in. Companies that invested millions compete to see who can bail out of the field most quickly. Now, as the new therapeutic approach enters the bust phase, industry support dries up and patients cannot benefit.

Fortunately, some novel therapies will make it to the third phase referred to above, that of redemption. Products are reengineered, and patient populations more likely to benefit are identified. As a critical mass of clinical validation accumulates, large biopharmaceutical companies start to consider whether to reenter the field; however, it takes true courage to be the first to head into a once-tainted field. It is at this moment in time that "validation" of the approach by a large biopharmaceutical company can change everything.

In the 1980s and 1990s, monoclonal antibodies went from being considered a "magic bullet" to being viewed by many experts as a dismal failure. With less than one month's cash remaining at Idec Pharmaceuticals, Bill Rastetter was able to convince Genentech scientists that they should be the first company to jump back into the monoclonal antibody arena with rituximab. The rest is history. Rituximab (Rituxan) has saved and improved countless lives, and has annual sales in the billions as one of the most successful cancer and immunology products in history. By 2008, there were eight monoclonal antibodies with annual sales of more than US$1 billion, with a total estimated worldwide market of $27 billion, including products such as trastuzumab (Herceptin) and bevacizumab (Avastin). The anti-angiogenesis approach went through all three cycles as well, with the field's father, Judah Folkman, relentlessly persevering toward redemption. Thanks to his determination, and that of others alongside him, bevacizumab, sorafenib (Nexavar), and sunitinib (Sutent) are approved therapies for colorectal, hepatocellular, and renal cell carcinomas, respectively.

In the oncolytic virotherapy field, the hurdles of the past are now being overcome with newly reengineered viruses with higher potency and systemic efficacy. Treatment regimens, including intravenous infusion and/or new combination therapies, have been introduced and optimized. Biopharmaceutical companies have taken notice. Over the past four years, Jennerex has reported regional partnerships in the European Union (Transgene, France), Korea (Green Cross), and China (Lee's Pharmaceuticals). None of these companies, however, is yet a household name

internationally, and these partnerships have not caught the attention of the field and its observers as has the Amgen move.

This promising field was just as promising the day before the Amgen announcement. Nevertheless, because science operates in the real, and very human, world we live in, the perception of this field has been fundamentally altered. We are in the messy and bumpy stage between the hatching of a captivating idea and the exploitation of that idea in the real world. In this stage, perception matters, and perception is reality. Today that perception has been markedly changed for the better. Let's hope that this story ends in true redemption for this field, the way it has for monoclonal antibodies and other successful novel therapies before it.

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